REMARKS

Applicants appreciate the thorough and detailed examination of the present application as evidenced by the Office Action dated June 22, 2007 (hereinafter, the "Office Action"). Applicants further appreciate the Examiner's comments and suggestions aimed to advance prosecution of the present application.

Claims 1-37 are pending in the present application, and Applicants acknowledge with appreciation that Claims 20-29, 31 and 32 are allowed and that Claims 8, 9, 11, 12, 15 and 33-37 are merely objected to as depending from a rejected base claim. Claims 1-7, 10, 12-14, 16-19 and 30 stand rejected.

Applicants provide the comments below to address the issues presented in the Office Action and in support of the patentability of the pending claims.

I. Oath/Declaration

The Office Action indicates that the oath or declaration is defective "because at page 1, the benefit of Provisional Application No. 60/444,536, filed February 21, 2003 is indicated. This serial number is incorrect and Office records indicate that the serial number should be '60/449,536,'" Office Action, page 2.

Applicants submit herewith a new Declaration and Power of Attorney in compliance with 37 C.F.R. §1.67(a) for the above-referenced application. The order of inventors' names as listed in the previous declaration has changed. Applicants further submit herewith an application data sheet and a Petition to Change Order of Inventors' Names under 37 C.F.R. §1.182.

II. Specification

The Office Action asserts that the disclosure is objected to because "page 1 does not contain a statement that a claim for benefit is made based on Provisional Application Serial No. 60/449,536, filed February 21, 2003." Office Action, page 2.

Applicants have amended the specification to correct a typographical error so that the statement of priority is correct. Accordingly, Applicants respectfully request that this objection to the specification be withdrawn.

III. Claim Objection

A. Claim 12

The Office Action states that Claim 12 is objected to "because at step '(c)', reference is incorrectly made to step '(c)' instead of a product produced by a previous step." Office Action, page 2.

Applicants have amended Claim 12 to include the appropriate reference to step "(b)". Accordingly, Applicants respectfully request that this objection to the specification be withdrawn.

B. Claims 8, 9, 11, 15 and 33-37

Claims 8, 9, 11, 15 and 33-37 stand objected to as depending from a rejected base claim. *See* Office Action, page 3. Applicants respectfully request that this objection be withdrawn at least in view of the reasons set forth under section V (Claim Rejections Under 35 U.S.C. § 103) of the present Amendment.

IV. Claim Rejections Under 35 U.S.C. §112, First Paragraph

Claims 13, 14, 16-19 and 30 stand rejected under 35 U.S.C. §112, first paragraph, as lacking enablement. More specifically, the Office Action asserts that the specification "while being enabling for the treatment of cancers disclosed in, for example, claim 15, does not reasonably provide enablement for the treatment of 'cancer' in general." Office Action, page 3.

In an effort to advance prosecution and facilitate allowance of the present application, as suggested by the Examiner, Applicants have amended Claims 13 and 30 to include the recitations of Claim 15. Accordingly, Applicants respectfully request that the rejections under 35 U.S.C. §112, first paragraph, be withdrawn.

V. Claim Rejections Under 35 U.S.C. § 103

Claims 1-7, 10 and 12 stand rejected under 35 U.S.C. §103 as being unpatentable over U.S. Patent Application Serial No. 2005/0181999 to Ferrandis et al. (hereinafter, "Ferrandis"). *See* Office Action, page 5.

The case law is clear with respect to obviousness. "A reference is considered in its entirety for what it clearly teaches to one skilled in the art." *In re Hedges*, 228 U.S.P.Q. 685,

686 (Fed. Cir. 1986). Additionally, the Court of Appeals for the Federal Circuit has further stated that, to support combining or modifying references, there must be **particular** evidence from the prior art as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed. *In re Kotzab*, 55 U.S.P.Q.2d 1313, 1317 (Fed. Cir. 2000).

Regarding Ferrandis, the Office Action states the following:

> Ferrandis et al. teach ***topical dermatological compositions*** comprising a ***sphingolipid, lactic acid and a solvent*** which may be an alcohol such as ethanol. Also, it is disclosed that the compositions are stable over time.
>
> The differences between the above and the claimed subject matter lies in that the ***reference fails to highlight each of the presently claimed sphingolipid compounds***, the present method of making the composition and the particular amounts/proportions of ingredients.
>
> However, the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to person having ordinary skill in the art to which the subject matter pertains because the reference teaches 'sphingolipids' in a non-limiting manner thus indicating that in order to practice the invention of the reference, ***one may select from the known sphingolipids and employ these compounds in the manner taught for 'sphingolipids***".

Office Action, pages 5 and 6 (emphasis added and citations omitted).

Applicants direct the Examiner's attention to the highlighted recitations. Concerning ***topical dermatological compositions***, Ferrandis describes topically applicable dermatological/cosmetic compositions suited for ungual/peri-ungual administration. *See* Abstract. In contrast, the formulations provided in the present application are suitable for parenteral and/or oral administration. As clearly recognized by one of ordinary skill in the art, the conditions for suitability for parenteral and/or oral administration differ from the conditions contributing to suitability for topical application. For example, considerations for parenteral and/or oral administration can include, among other things, a higher degree of solubility, tonicity adjustment and purity as compared to topical administration. Moreover, parenteral and oral administration are typically employed to provide systemic effects in contrast to topical administration which is seldom employed to provide systemic effects due to, among other things, erratic absorption which can be associated with topical administration. Topical formulations, such as those described in Ferrandis, may be solid, semi-solid or viscous liquids at body temperature and may further include water-insoluble

ingredients, and thus, such topical formulations are suitable for external body use only. Direct injection of a solid, semi-solid and even viscous liquid, irrespective of other water insoluble components, into the veins or arteries of the body may constitute a thrombotic and/or embolic event to the systemic blood vessels, particularly the blood vessels of the lung (i.e., the pulmonary vascular bed), both of which events are medically contraindicated, as they may result in morbidity and/or mortality.

The Office Action asserts that the Ferrandis topical formulations include a ***sphingolipid, lactic acid and a solvent*** which may be an alcohol such as ethanol. Applicants respectfully submit that the topical formulations described in Ferrandis include: (a) at least one biologically active agent (e.g., antifungal) and (b) at least two of the pro-penetrating agents selected from the group consisting of urea, an organic acid and an ethoxydiglycol, the at least two-pro-penetrating agents respectively being present in effective amounts as to synergistically improve the ungual/peri-ungual bioavailability of the at least one biologically active agent. At paragraph [0056], Ferrandis states that the solutions for ungual and peri-ungual applications **may** also include a laundry list of additives, one of which is sphingolipids. Thus, not only does Ferrandis fail to teach ***each of the presently claimed sphingolipid compounds***, Ferrandis fails to generally teach or suggest a sphingolipid formulation or methods of making the same. The mere use of a sphingolipid as an additive does not teach or suggest to one of ordinary skill in the art the use of a sphingolipid as a major component of a formulation.

The Office Action asserts that ***one may select from the known sphingolipids and employ these compounds in the manner taught for sphingolipids.*** From the disclosure provided by Ferrandis, after extensive picking and choosing, one of ordinary skill in the art may be led to employ sphingolipids as an **additive** in **topical formulations** for **ungual/peri-ungual administration**. Relying upon Ferrandis entails far more than a determination of an optimum dosage regimen to employ the presently claimed invention. The selection of components of the formulation using Ferrandis as a guide would entail undue experimentation where sphingolipids are not the active ingredients in the Ferrandis formulation, but a mere additive selected from a laundry list of possibilities. Thus, Applicants respectfully submit that the Office Action employs impermissible hindsight by using the Applicants' disclosure as a guide to reconstruct the claimed invention.

Accordingly, Applicants respectfully request that the rejections under 35 U.S.C. §103 be withdrawn.

Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully request that all outstanding rejections to the claims be withdrawn and that a Notice of Allowance be issued in due course.

If, in the opinion of the Examiner, a telephonic conference would expedite the examination of this matter, the Examiner is invited to call the undersigned attorney at (919) 854-1400.

Respectfully submitted,

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CERTIFICATION OF TRANSMISSION

I hereby certify that this correspondence is being transmitted via the Office electronic filing system in accordance with § 1.6(a)(4) to the U.S. Patent and Trademark Office on September 24, 2007.

Laneisha C. Hayes
Date of Signature: September 24, 2007